

Initial REMS Approval: 6/2010
Most Recent Modification: 10/2014

BLA 125166/172 SOLIRIS[®] (ECULIZUMAB)

RECOMBINANT HUMANIZED MONOCLONAL ANTIBODY

Alexion Pharmaceuticals, Inc.

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Cheshire, CT 06410

(203) 272-2596

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S)

The goals of the REMS are:

- To mitigate the occurrence and morbidity associated with meningococcal infections
- To educate Healthcare Professionals (HCPs) and Patients (or Caregivers, or Legal Guardians) regarding:
 - the increased risk of meningococcal infections with Soliris
 - the early signs of invasive meningococcal infections, and
 - the need for immediate medical evaluation of signs and symptoms consistent with possible meningococcal infections

II. REMS ELEMENTS

A. Medication Guide

Alexion will ensure that a Medication Guide is dispensed with each prescription of Soliris and in accordance with 21 CFR 208.24.

The Medication Guide is part of the REMS and is appended.

B. Elements to Assure Safe Use

Healthcare providers who prescribe Soliris are specially certified.

- a. Prescriber certification is based on prescriber agreement that the prescriber will:
 - i) Counsel patients and provide the patient educational materials to the patient, including the Soliris Patient Safety Card and the Medication Guide
 - ii) Provide the Medication Guide to the patient prior to each infusion
 - iii) Review the educational materials (Soliris Patient Safety Card, Prescriber Introductory Letter, Prescriber Safety Brochure *Important Safety Information about Soliris*, Patient Safety Brochure *Important Safety Information about Soliris*, and Dosing and Administration Guide) and the product labeling and comply with the directions for safe use including ensuring patients receive a meningococcal vaccine.
 - iv) Promptly report to Alexion at 1-888-765-4747 or to the FDA at 1-800-332-1088 or 1-800-300-43874 (serious life-threatening) cases of meningococcal infection, including the patients' clinical outcomes
- b. The prescriber will fax the completed enrollment form to 1-877-580-2596 (ALXN), email the completed form to OSSP@alxn.com, or mail the form to Alexion Pharmaceuticals, Inc.; Attn: OneSource Safety Support Program; 352 Knotter Drive, Cheshire, CT 06410,. A prescriber may also complete the enrollment by phone with Alexion at 1-888-765-4747 or obtain enrollment documents via the Soliris REMS website at www.SolirisREMS.com. A prescriber may also complete the enrollment on the internet via the Soliris REMS-dedicated website at www.SolirisREMS.com.
- c. Alexion will contact certified prescribers every year to provide the educational materials (Medication Guide, Soliris Patient Safety Card, Prescriber Safety Brochure, and *Important Safety Information about Soliris*, Patient Safety Brochure, *Important Safety Information about Soliris*, and Dosing and Administration Guide). The educational materials and enrollment form will also be available on a REMS-dedicated webpage at www.SolirisREMS.com. The REMS-dedicated website (www.SolirisREMS.com) will be accessible directly or from a link from www.soliris.net.
- d. The following materials are part of the REMS and are appended
 - (1) Soliris Patient Safety Card
 - (2) Prescriber Introductory Letter and Enrollment Form
 - (3) Patient Safety Brochure, *Important Safety Information about Soliris*

- (4) Prescriber Safety Brochure, *Important Safety Information about Soliris*
 - (5) Dosing and Administration Guide
 - (6) Soliris REMS website (SolirisREMS.com)
- e. Alexion will maintain a database of certified prescribers in the REMS program, and will ensure that Soliris is distributed only to certified prescribers. Alexion will ensure that prescribers comply with the requirements of the REMS Program.

C. Timetable for Submission of Assessments

REMS assessments will be submitted to the FDA every two years with the next report to be submitted by June 1, 2015. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Alexion will submit each assessment so that it will be received by the FDA on or before the due date.

MEDICATION GUIDE

Soliris® (so-leer-is)
(eculizumab)

Read the Medication Guide before you start Soliris and before each infusion. This Medication Guide does not take the place of talking with your doctor about your medical condition or your treatment. Talk to your doctor if you have any questions about your treatment with Soliris.

What is the most important information I should know about Soliris?

Soliris is a medicine that affects your immune system. Soliris can lower the ability of your immune system to fight infections.

- **Soliris increases your risk of getting serious and life-threatening meningococcal infections.**

Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

1. **You must receive a meningococcal vaccine at least 2 weeks before your first dose of Soliris unless you have already had this vaccine. If your doctor decides that urgent treatment with Soliris is needed, you should receive a meningococcal vaccine as soon as possible.**
2. **If you had a meningococcal vaccine in the past, you might need a booster dose before starting Soliris. Your doctor will decide if you need another dose of a meningococcal vaccine.**
3. **A meningococcal vaccine does not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection:**
 - **headache with nausea or vomiting**
 - **headache and a fever**
 - **headache with a stiff neck or stiff back**
 - **fever of 103° F (39.4° C) or higher**

- **fever and a rash**
- **confusion**
- **muscle aches with flu-like symptoms**
- **eyes sensitive to light**

Your doctor will give you a **Patient Safety Card** about the risk of meningococcal infection. Carry it with you at all times during treatment and for 3 months after your last Soliris dose. Your risk of meningococcal infection may continue for several weeks after your last dose of Soliris. It is important to show this card to any doctor or nurse who treats you. This will help them diagnose and treat you quickly.

Soliris is only available through a program called the Soliris REMS. Before you can receive Soliris, your doctor must:

- enroll in the Soliris REMS program
- counsel you about the risk of meningococcal infection
- give you information about the symptoms of meningococcal infection
- give you a **Patient Safety Card** about your risk of meningococcal infection, as discussed above.
- make sure that you are vaccinated with a meningococcal vaccine

Soliris may also increase the risk of other types of serious infections. If your child is treated with Soliris, make sure that your child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib).

What is Soliris?

Soliris is a prescription medicine called a monoclonal antibody. Soliris is used to treat people with:

- a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). PNH affects red blood cells.
- a disease called atypical Hemolytic Uremic Syndrome (aHUS). aHUS affects the blood system, kidney, and sometimes other body organs.

Soliris works by blocking part of your immune system. This can help your symptoms but it can also increase your chance for infection.

It is important that you:

- have all recommended vaccinations before you start Soliris
- stay up-to-date with all recommended vaccinations during treatment with Soliris

Who should not receive Soliris?

Do not receive Soliris if you:

- have a meningococcal infection
- have not been vaccinated against meningitis infection, unless your doctor decides that urgent treatment with Soliris is needed. See "What is the most important information I should know about Soliris?"

What should I tell my doctor before receiving Soliris?

Before receiving Soliris, tell your doctor if you:

- have an infection or fever
- are pregnant or plan to become pregnant. It is not known if Soliris will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Soliris passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How will I receive Soliris?

- Soliris is given through a vein (I.V. or intravenous infusion) usually over 35 minutes in adults and 1-4 hours in pediatric patients. If you have an allergic reaction during your Soliris infusion, your doctor may decide to give Soliris more slowly or stop your infusion.
- If you are an adult, you will usually receive a Soliris infusion by your doctor:

weekly for five weeks, then
every 2 weeks

- If you are less than 18 years of age, your doctor will decide how often you will receive Soliris depending on your age and body weight.
- After each infusion, you should be monitored for one hour for allergic reactions. See “What are the possible side effects of Soliris?”
- If you forget or miss a Soliris infusion, call your doctor right away.
- **If you have PNH, your doctor will need to monitor you closely for at least 8 weeks after stopping Soliris. Stopping treatment with Soliris may cause breakdown of your red blood cells due to PNH.**

Symptoms or problems that can happen due to red blood cell breakdown include:

- drop in the number of your red blood cell count
 - drop in your platelet count
 - confusion
 - chest pain
 - kidney problems
 - blood clots
 - difficulty breathing
- **If you have aHUS, your doctor will need to monitor you closely during and for at least 12 weeks after stopping treatment for signs of worsening aHUS symptoms or problems related to abnormal clotting (thrombotic microangiopathy).**

Symptoms or problems that can happen with abnormal clotting may include:

- stroke
- confusion
- seizures
- chest pain (angina)
- difficulty breathing
- kidney problems
- swelling in arms or legs
- a drop in your platelet count

What are the possible side effects of Soliris?

Soliris can cause serious side effects, including:

- See “What is the most important information I should know about Soliris?”

- **Serious allergic reactions.** Serious allergic reactions can happen during your Soliris infusion. Tell your doctor or nurse right away if you get any of these symptoms during your Soliris infusion:
 - chest pain
 - trouble breathing or shortness of breath
 - swelling of your face, tongue, or throat
 - feel faint or pass out

If you have an allergic reaction to Soliris, your doctor may need to infuse Soliris more slowly, or stop Soliris. See "How will I receive Soliris?"

Common side effects in people with PNH treated with Soliris include:

- headaches
- runny nose and colds
- sore throat
- back pain
- nausea

Common side effects in people with aHUS treated with Soliris include:

- headache
- diarrhea
- hypertension
- common cold (upper respiratory infection)
- abdominal pain
- vomiting
- nasopharyngitis
- anemia
- cough
- peripheral edema

- nausea
- urinary tract infections
- pyrexia

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of Soliris. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about Soliris

Medicines are sometimes prescribed for conditions other than those listed in a Medication Guide. This Medication Guide summarizes the most important information about Soliris. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Soliris that is written for healthcare professionals.

What are the ingredients in Soliris?

Active ingredient: eculizumab

Inactive ingredients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 (vegetable origin) and Water for Injection.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by Alexion Pharmaceuticals, Inc. 352 Knotter Drive, Cheshire, CT 06410 USA.

Revised: 04/2014

DOSING AND ADMINISTRATION GUIDE

PNH | aHUS

For Paroxysmal Nocturnal Hemoglobinuria (**PNH**) and atypical Hemolytic Uremic Syndrome (**aHUS**) patients

Dosing and Administration

Soliris is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

Soliris is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement mediated thrombotic microangiopathy.

Limitation of Use

Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS).

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

See full prescribing information for complete boxed warning

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris.

Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See Serious Meningococcal Infections for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747).

Indications and usage

Soliris is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

Soliris is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Limitation of Use

Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS).

Adverse reactions

The most frequently reported adverse reactions in the PNH randomized trial ($\geq 10\%$ overall and greater than placebo) are: headache, nasopharyngitis, back pain, and nausea.

The most frequently reported adverse reactions in aHUS single arm prospective trials ($\geq 20\%$ combined per patient incidence) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections and pyrexia.

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

For patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)
Soliris® (eculizumab) PNH Dosing Guide

All patients must be vaccinated against *Neisseria meningitidis* at least 2 weeks prior to the first dose of Soliris therapy. Do not initiate Soliris therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not currently vaccinated, unless the risks of delaying Soliris treatment outweigh the risk of developing a meningococcal infection.¹

Soliris: a chronic therapy for a chronic disease^{1,2}

PNH Dosing Schedule for Patients >18 years										
Pretreatment		Induction Phase				Maintenance Phase				
≥ 2 weeks before induction	Week	1	2	3	4	5	6	7	8	9+
<i>Neisseria meningitidis</i> vaccination	Soliris dose	600 mg	600 mg	600 mg	600 mg	900 mg	X	900 mg	X	900 mg

q14d

Soliris should be administered at the recommended dosage regimen time points, or within two days of these time points.

Soliris should be administered at the recommended dosing interval or within 2 days before or after these time points.

- Fixed dose on time is critical to control chronic, complement-mediated hemolysis; for breakthrough hemolysis, dosing may be adjusted to every 12 days instead of 14 days¹
- No dosing adjustments recommended based on age, gender, race, or renal insufficiency¹
- Premedications are not routinely required

Monitoring after Discontinuation

Monitor patients after discontinuing Soliris for at least 8 weeks to detect hemolysis.

Important Administration Information

Soliris must be diluted to a final admixture concentration of 5 mg/mL prior to administration.

The diluted solution is a clear, colorless liquid and should be practically free of any particles.

DO NOT ADMINISTER AS AN IV PUSH OR BOLUS INJECTION.

- If diluted solution is refrigerated, warm to room temperature (18°C-25°C [64°F-77°F]) only by exposure to ambient air
- Administer as an IV infusion over 35 minutes in adults and 1-4 hours in pediatric patients via gravity feed, a syringe-type pump, or an infusion pump
- It is not necessary to protect diluted solution from light during administration

To learn more about Soliris, please call 1.888.SOLIRIS (1.888.765.4747) or visit www.Soliris.net. To learn more about Soliris REMS, please call 1.888.SOLIRIS (1.888.765.4747) or visit www.SolirisREMS.com.

For patients with atypical Hemolytic Uremic Syndrome (aHUS)
Soliris® (eculizumab) aHUS Dosing Guide

All patients must be vaccinated against *Neisseria meningitidis* at least 2 weeks prior to the first dose of Soliris therapy. Do not initiate Soliris therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not currently vaccinated, unless the risks of delaying Soliris treatment outweigh the risk of developing a meningococcal infection.¹

Soliris is a therapy for aHUS—a chronic disease needing chronic treatment¹

aHUS Adult (≥18 years of age) Dosing Schedule ¹										
Pretreatment		Induction Phase				Maintenance Phase				
≥2 weeks before induction	Week	1	2	3	4	5	6	7	8	9+
<i>Neisseria meningitidis</i> vaccination	Soliris dose	900 mg	900 mg	900 mg	900 mg	1200 mg	—	1200 mg	—	1200 mg

q14d

aHUS Weight-Based Dosing Schedule for Patients <18 Years ¹		
Body Weight	Induction Phase	Maintenance Phase
40 kg and over	900 mg weekly × 4 doses	1200 mg at week 5; then 1200 mg every 2 weeks
30 kg to less than 40 kg	600 mg weekly × 2 doses	900 mg at week 3; then 900 mg every 2 weeks
20 kg to less than 30 kg	600 mg weekly × 2 doses	600 mg at week 3; then 600 mg every 2 weeks
10 kg to less than 20 kg	600 mg weekly × 1 dose	300 mg at week 2; then 300 mg every 2 weeks
5 kg to less than 10 kg	300 mg weekly × 1 dose	300 mg at week 2; then 300 mg every 3 weeks

Soliris should be administered at the recommended dosing interval or within 2 days before or after these time points.

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

Supplemental Dosing of Soliris Is Required for Patients Undergoing Concomitant Plasma Therapy¹

Type of Intervention	Most Recent Soliris Dose	Supplemental Soliris Dose With Each PE/PI Intervention	Timing of Supplemental Soliris Dose
Plasmapheresis or plasma exchange	300 mg	300 mg per each plasmapheresis or plasma exchange session	Within 60 minutes after each plasmapheresis or plasma exchange
	600 mg or more	600 mg per each plasmapheresis or plasma exchange session	
Fresh frozen plasma infusion	300 mg or more	300 mg per infusion of fresh frozen plasma	60 minutes prior to each infusion of fresh frozen plasma

Monitoring after Discontinuation

Thrombotic microangiopathy (TMA) complications after discontinuation were observed in the aHUS clinical studies.¹

aHUS patients who discontinue treatment with Soliris should be monitored closely for at least 12 weeks for signs and symptoms of TMA complications. If TMA complications occur after Soliris discontinuation, consider reinstitution of Soliris treatment, plasma therapy,[†] or appropriate organ-specific supportive measures.¹

DO NOT ADMINISTER AS AN IV PUSH OR BOLUS INJECTION.

- If diluted solution is refrigerated, warm to room temperature (18°C-25°C [64°F-77°F]) only by exposure to ambient air
- Administer as an IV infusion over 35 minutes in adults and 1-4 hours in pediatric patients via gravity feed, a syringe-type pump, or an infusion pump
- It is not necessary to protect diluted solution from light during administration

To learn more about Soliris, please call 1.888.SOLIRIS (1.888.765.4747) or visit www.Soliris.net. To learn more about Soliris REMS, please call 1.888.SOLIRIS (1.888.765.4747) or visit www.SolirisREMS.com.

[†]Plasma therapy = plasmapheresis, plasma exchange, or fresh frozen plasma infusion (PE/PI).

For PNH and aHUS

Preparation of Soliris® (eculizumab) for Administration¹

All patients must be vaccinated against *Neisseria meningitidis* at least 2 weeks prior to the first dose of Soliris therapy. Do not initiate Soliris therapy in patients with unresolved serious *Neisseria meningitidis* infection or who are not currently vaccinated, unless the risks of delaying Soliris treatment outweigh the risk of developing a meningococcal infection.¹

Soliris Dose	Diluent Volume	Final Volume
300 mg	30 mL	50 mL
600 mg	60 mL	120 mL
900 mg	90 mL	180 mL
1200 mg	120 mL	240 mL

1. Withdraw the required amount of Soliris from the vial into a sterile syringe and transfer the recommended dose to an infusion bag.
2. Dilute Soliris to a final concentration of 5 mg/mL using the above table as a guideline. The volume of diluent should be equivalent to the drug volume.
3. Gently invert the infusion bag containing the diluted solution to ensure thorough mixture of the product and the diluent
 - Discard any unused portion left in the vial, as the product contains no preservatives.
4. Inspect visually for particulate matter and discoloration prior to administration
 - The diluted solution is a clear colorless liquid and should be practically free of any particles.
5. Allow the admixture to adjust to room temperature prior to administration (18°C-25°C, 64°F-77°F). **It must not be heated in a microwave or with any heat source other than ambient air temperature.**
6. Admixed solution of Soliris is stable for 24 hours at 2°C-8°C (36°F-46°F) and at room temperature.

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

How Supplied, Storage, and Distribution¹

- Vial—30 mL, liquid
- Product strength—10 mg/mL
- Product count—300 mg/30 mL (vial)
- Product physical specs—1 vial per carton
 - Shipped just in time for infusion
 - Weight: <1 lb
 - Dimensions: 1.625" × 1.625" × 3.125"
- Must be stored in the original carton until time of use under conditions at 2°C-8°C (36°F-46°F)
- Protect from light
- DO NOT FREEZE; DO NOT SHAKE
- Do not infuse beyond the expiration date stamped on the carton
- NDC 25682-001-01: Each single-unit carton contains one 30-mL vial of Soliris (10 mg/mL)

To enroll in the Soliris REMS and order Soliris, please call 1.888.SOLIRIS (1.888.765.4747). To learn more about Soliris REMS, please call 1.888.SOLIRIS (1.888.765.4747) or visit SolirisREMS.com. The completed Prescriber Enrollment Form can be faxed to the Soliris OneSource Safety Support Program (OSSP) at 1.877.580.2596 (ALXN); scanned and e-mailed to OSSP@alxn.com; or mailed to Alexion Pharmaceuticals, Inc., 352 Knotter Drive, Cheshire, CT 06410. Enrollment can also be completed online at SolirisREMS.com.

Contact Soliris OneSource at 1.888.SOLIRIS (1.888.765.4747)

- All Alexion Nurse Case Managers are registered nurses and have extensive insurance and clinical experience. An Alexion Nurse Care Manager will partner with each patient and his or her healthcare team
- Fast and convenient same-day shipping that meets the needs of PNH and aHUS patients

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

See full prescribing information for complete boxed warning

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris.

Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See Serious Meningococcal Infections for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747).

Please see enclosed full Prescribing Information for Soliris, including Boxed WARNING regarding serious meningococcal infection.

References: 1. Soliris® [package insert]. Cheshire, CT: Alexion Pharmaceuticals, Inc; 2014. 2. Helley D, de Latour RP, Porcher R, et al; French Society of Hematology. Evaluation of hemostasis and endothelial function in patients with paroxysmal nocturnal hemoglobinuria receiving eculizumab. *Haematologica*. 2010;95:574-581.

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PATIENT SAFETY CARD

PATIENT SAFETY INFORMATION CARD



Important Safety Information for Patients Taking Soliris®

Soliris can lower the ability of your immune system to fight infections, **especially meningococcal infection, which requires immediate medical attention.** If you experience any of the following symptoms, you should immediately call your doctor or seek emergency medical care, preferably in a major emergency medical care center:

- headache with nausea or vomiting
- headache and a fever
- headache with a stiff neck or stiff back
- fever of 103°F (39.4°C) or higher
- fever and a rash
- confusion
- muscle aches with flu-like symptoms
- eyes sensitive to light



Get emergency medical care right away if you have any of these signs or symptoms and show this card.

Even if you stop using Soliris, keep this card with you for 3 months after your last Soliris dose. Your risk of meningococcal infection may continue for several weeks after your last dose of Soliris.

PATIENT SAFETY INFORMATION CARD


Information for the Treating Physician



This patient has been prescribed Soliris® (eculizumab) therapy, which increases the patient's susceptibility to meningococcal infection (*Neisseria meningitidis*) or other general infections.

- Meningococcal infections may become rapidly life-threatening or fatal if not recognized and treated early
- **Evaluate immediately if infection is suspected and treat with appropriate antibiotics if necessary**
- Contact prescribing physician (below) as soon as possible

For more information about Soliris, please refer to the full Prescribing Information. In case of safety concerns, call **1.888.SOLIRIS (1.888.765.4747)**.

 **Patients receiving Soliris should carry this card at all times. Show this card to any doctor involved in your health care.**

Patient Name _____

Prescriber Name _____

Prescriber Number _____


SOLIRIS[®]
(e c u l i z u m a b)

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PATIENT SAFETY BROCHURE; IMPORTANT SAFETY INFORMATION FOR PATIENTS

Before starting on Soliris® Important safety information for patients

Before you begin Soliris® (eculizumab) treatment, your physician will give you a:

- Medication Guide
- Soliris Patient Safety Information Card

Read this information and ask your physician any questions you may have about Soliris at any time. Your physician will be able to provide you with the best education and support.

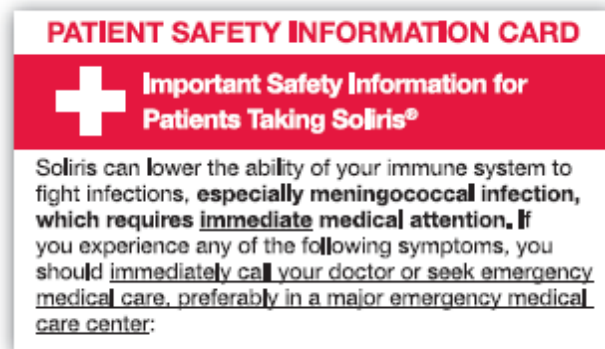
Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

Patient Safety Information Card

You will receive a Patient Safety Information Card from your doctor that lists symptoms of a meningococcal infection and what to do if you have one. Your doctor should discuss with you the importance and the proper use of this card.

Carry this card at all times and show it to any healthcare professional who treats you. Seek immediate treatment for headache with nausea or vomiting, or headache with fever, even if you do not have your Patient Safety Information Card with you. Your Patient Safety Information Card contains safety guidance for you and your healthcare providers.



Soliris OneSource™ Treatment Support Program

Soliris OneSource is a program offered by Alexion that provides education; assistance with funding options and access to Soliris; and ongoing treatment support for people living with PNH or aHUS, and their caregivers. OneSource is staffed by Alexion Nurse Case Managers who are registered nurses with healthcare and insurance expertise. Alexion Pharmaceuticals developed this program to help make disease awareness and treatment access as easy as possible for you and your healthcare team.

Questions about PNH, aHUS, or Soliris? Just call OneSource at 1.888.SOLIRIS (1.888.765.4747) to speak with an Alexion Nurse Case Manager.

For Discussion with Patients—Important Safety Information

MEDICATION GUIDE **Soliris® (so-leer-is)** **(eculizumab)**

Read the Medication Guide before you start Soliris and before each infusion. This Medication Guide does not take the place of talking with your doctor about your medical condition or your treatment. Talk to your doctor if you have any questions about your treatment with Soliris.

What is the most important information I should know about Soliris?

Soliris is a medicine that affects your immune system. Soliris can lower the ability of your immune system to fight infections.

- **Soliris increases your risk of getting serious and life-threatening meningococcal infections**

Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

- **You must receive a meningococcal vaccine at least 2 weeks before your first dose of Soliris unless you have already had this vaccine. If your doctor decides that urgent treatment with Soliris is needed, you should receive a meningococcal vaccine as soon as possible.**
- **If you had a meningococcal vaccine in the past, you might need a booster dose before starting Soliris. Your doctor will decide if you need another dose of a meningococcal vaccine.**
- **A meningococcal vaccine does not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection:**
 - headache with nausea or vomiting
 - headache and a fever
 - headache with a stiff neck or stiff back
 - fever of 103°F (39.4°C) or higher
 - fever and a rash
 - confusion
 - muscle aches with flu-like symptoms
 - eyes sensitive to light

Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

Your doctor will give you a **Patient Safety Card** about the risk of meningococcal infection. Carry it with you at all times during treatment and for 3 months after your last Soliris® dose. Your risk of meningococcal infection may continue for several weeks after your last dose of Soliris. It is important to show this card to any doctor or nurse who treats you. This will help them diagnose and treat you quickly.

Soliris is only available through a program called the Soliris REMS. Before you can receive Soliris, your doctor must:

- enroll in the Soliris REMS program
- counsel you about the risk of meningococcal infection
- give you information about the symptoms of meningococcal infection
- give you a **Patient Safety Card** about your risk of meningococcal infection, as discussed above.
- make sure that you are vaccinated with a meningococcal vaccine

Soliris may also increase the risk of other types of serious infections. If your child is treated with Soliris, make sure that your child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib).

What is Soliris?

Soliris is a prescription medicine called a monoclonal antibody. Soliris is used to treat people with:

- a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). PNH affects red blood cells.
- a disease called atypical Hemolytic Uremic Syndrome (aHUS). aHUS affects the blood system, kidney, and sometimes other body organs.

Soliris works by blocking part of your immune system. This can help your symptoms but it can also increase your chance for infection.

It is important that you:

- have all recommended vaccinations before you start Soliris
- stay up-to-date with all recommended vaccinations during treatment with Soliris

For Discussion with Patients—Important Safety Information (continued)

Who should not receive Soliris®?

Do not receive Soliris if you:

- have a meningococcal infection
- have not been vaccinated against meningitis infection, unless your doctor decides that urgent treatment with Soliris is needed. See “What is the most important information I should know about Soliris?”

What should I tell my doctor before receiving Soliris?

Before receiving Soliris, tell your doctor if you:

- have an infection or fever
- are pregnant or plan to become pregnant. It is not known if Soliris will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Soliris passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How will I receive Soliris?

- Soliris is given through a vein (I.V. or intravenous infusion) usually over 35 minutes in adults and 1-4 hours in pediatric patients. If you have an allergic reaction during your Soliris infusion, your doctor may decide to give Soliris more slowly or stop your infusion.
- If you are an adult, you will usually receive a Soliris infusion by your doctor:
 - weekly for five weeks, then
 - every 2 weeks
- If you are less than 18 years of age, your doctor will decide how often you will receive Soliris depending on your age and body weight.
- After each infusion, you should be monitored for one hour for allergic reactions. See “What are the possible side effects of Soliris?”
- If you forget or miss a Soliris infusion, call your doctor right away.

Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

- **If you have PNH, your doctor will need to monitor you closely for at least 8 weeks after stopping Soliris®. Stopping treatment with Soliris may cause breakdown of your red blood cells due to PNH.**
Symptoms or problems that can happen due to red blood cell breakdown include:
 - drop in the number of your red blood cell count
 - drop in your platelet count
 - confusion
 - chest pain
 - kidney problems
 - blood clots
 - difficulty breathing
- **If you have aHUS, your doctor will need to monitor you closely during and for at least 12 weeks after stopping treatment for signs of worsening aHUS symptoms or problems related to abnormal clotting (thrombotic microangiopathy).**
Symptoms or problems that can happen with abnormal clotting may include:
 - stroke
 - confusion
 - seizures
 - chest pain (angina)
 - difficulty breathing
 - kidney problems
 - swelling in arms or legs
 - a drop in your platelet count

What are the possible side effects of Soliris?

Soliris can cause serious side effects, including:

- **See “What is the most important information I should know about Soliris?”**
- **Serious allergic reactions.** Serious allergic reactions can happen during your Soliris infusion. Tell your doctor or nurse right away if you get any of these symptoms during your Soliris infusion:
 - chest pain
 - trouble breathing or shortness of breath
 - swelling of your face, tongue, or throat
 - feel faint or pass out

If you have an allergic reaction to Soliris, your doctor may need to infuse Soliris more slowly, or stop Soliris. See “How will I receive Soliris?”

For Discussion with Patients—Important Safety Information (continued)

Common side effects in people with PNH treated with Soliris® include:

- headaches
- runny nose and colds
- sore throat
- back pain
- nausea

Common side effects in people with aHUS treated with Soliris include:

- headache
- diarrhea
- high blood pressure
- common cold (upper respiratory infection)
- abdominal pain
- vomiting
- nasopharyngitis
- low red blood cell count
- cough
- peripheral edema
- nausea
- urinary tract infection
- pyrexia

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of Soliris. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1.800.FDA.1088.

Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

General information about Soliris®

Medicines are sometimes prescribed for conditions other than those listed in a Medication Guide. This Medication Guide summarizes the most important information about Soliris. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Soliris that is written for healthcare professionals.

What are the ingredients in Soliris?

Active ingredient: eculizumab

Inactive ingredients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 (vegetable origin) and Water for Injection.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by Alexion Pharmaceuticals, Inc.
352 Knotter Drive, Cheshire, CT 06410 USA.

Revised: 09/2014

Want to learn more about Soliris®?

- Visit www.Soliris.net or www.SolirisREMS.com
- Call 1.888.SOLIRIS (1.888.765.4747) for information regarding Soliris and the Soliris REMS

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See Serious Meningococcal Infections for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747).

The most frequently reported adverse reactions in the PNH randomized trial ($\geq 10\%$ overall and greater than placebo) are: headache, nasopharyngitis, back pain, and nausea.

The most frequently reported adverse reactions in aHUS single arm prospective trials ($\geq 20\%$ combined per patient incidence) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia.

Please see full Prescribing Information for Soliris, including boxed WARNING regarding serious meningococcal infection.

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PRESCRIBER SAFETY BROCHURE; IMPORTANT SAFETY INFORMATION FOR THE HEALTHCARE PROVIDER

BEFORE STARTING YOUR PATIENTS ON SOLIRIS®

Important safety information for the healthcare provider

Prior to initiating Soliris® (eculizumab) therapy, it's important to review with patients the *Soliris Patient Safety Information Card* and instruct them to be diligent and follow the safety information. Encourage your patients to ask any questions they may have about Soliris at any time. Your patients will come to you for the answers, so provide them with the best education and support you can by becoming better acquainted with Soliris safety information.

These tools are to aid you in your discussions. In our ongoing effort to maximize the safety and improve outcomes we have provided safety resources, including:

- Patient Safety Information Card
- A Soliris Medication Guide for you and your patients

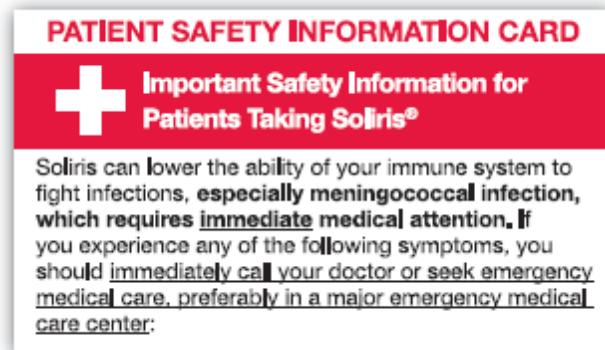
Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

Patient Safety Information Card

You are provided with Patient Safety Information Cards to give to your patients. You should discuss the importance and the proper use of this card with every patient. Patients should carry this card at all times to show to any healthcare professional involved in their care. The Patient Safety Information Card contains safety guidance for Soliris patients and their healthcare providers.

Prescribers should advise patients to seek medical attention immediately if they develop headache with nausea or vomiting, or headache and fever, even if they don't have their Patient Safety Information Card with them.



For Discussion with Patients—Important Safety Information

MEDICATION GUIDE **Soliris® (so-leer-is)** **(eculizumab)**

Read the Medication Guide before you start Soliris and before each infusion. This Medication Guide does not take the place of talking with your doctor about your medical condition or your treatment. Talk to your doctor if you have any questions about your treatment with Soliris.

What is the most important information I should know about Soliris?

Soliris is a medicine that affects your immune system. Soliris can lower the ability of your immune system to fight infections.

- **Soliris increases your risk of getting serious and life-threatening meningococcal infections**

Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

- **You must receive a meningococcal vaccine at least 2 weeks before your first dose of Soliris unless you have already had this vaccine. If your doctor decides that urgent treatment with Soliris is needed, you should receive a meningococcal vaccine as soon as possible.**
- **If you had a meningococcal vaccine in the past, you might need a booster dose before starting Soliris. Your doctor will decide if you need another dose of a meningococcal vaccine.**
- **A meningococcal vaccine does not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection:**
 - headache with nausea or vomiting
 - headache and a fever
 - headache with a stiff neck or stiff back
 - fever of 103°F (39.4°C) or higher
 - fever and a rash
 - confusion
 - muscle aches with flu-like symptoms
 - eyes sensitive to light

Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

Your doctor will give you a **Patient Safety Card** about the risk of meningococcal infection. Carry it with you at all times during treatment and for 3 months after your last Soliris® dose. Your risk of meningococcal infection may continue for several weeks after your last dose of Soliris. It is important to show this card to any doctor or nurse who treats you. This will help them diagnose and treat you quickly.

Soliris is only available through a program called the Soliris REMS. Before you can receive Soliris, your doctor must:

- enroll in the Soliris REMS program
- counsel you about the risk of meningococcal infection
- give you information about the symptoms of meningococcal infection
- give you a **Patient Safety Card** about your risk of meningococcal infection, as discussed above.
- make sure that you are vaccinated with a meningococcal vaccine

Soliris may also increase the risk of other types of serious infections. If your child is treated with Soliris, make sure that your child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib).

What is Soliris?

Soliris is a prescription medicine called a monoclonal antibody. Soliris is used to treat people with:

- a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). PNH affects red blood cells.
- a disease called atypical Hemolytic Uremic Syndrome (aHUS). aHUS affects the blood system, kidney, and sometimes other body organs.

Soliris works by blocking part of your immune system. This can help your symptoms but it can also increase your chance for infection.

It is important that you:

- have all recommended vaccinations before you start Soliris
- stay up-to-date with all recommended vaccinations during treatment with Soliris

For Discussion with Patients—Important Safety Information (continued)

Who should not receive Soliris®?

Do not receive Soliris if you:

- have a meningococcal infection
- have not been vaccinated against meningitis infection, unless your doctor decides that urgent treatment with Soliris is needed. See “What is the most important information I should know about Soliris?”

What should I tell my doctor before receiving Soliris?

Before receiving Soliris, tell your doctor if you:

- have an infection or fever
- are pregnant or plan to become pregnant. It is not known if Soliris will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Soliris passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How will I receive Soliris?

- Soliris is given through a vein (I.V. or intravenous infusion) usually over 35 minutes in adults and 1-4 hours in pediatric patients. If you have an allergic reaction during your Soliris infusion, your doctor may decide to give Soliris more slowly or stop your infusion.
- If you are an adult, you will usually receive a Soliris infusion by your doctor:
 - weekly for five weeks, then
 - every 2 weeks
- If you are less than 18 years of age, your doctor will decide how often you will receive Soliris depending on your age and body weight.
- After each infusion, you should be monitored for one hour for allergic reactions. See “What are the possible side effects of Soliris?”
- If you forget or miss a Soliris infusion, call your doctor right away.

Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

- **If you have PNH, your doctor will need to monitor you closely for at least 8 weeks after stopping Soliris®. Stopping treatment with Soliris may cause breakdown of your red blood cells due to PNH.**
Symptoms or problems that can happen due to red blood cell breakdown include:
 - drop in the number of your red blood cell count
 - drop in your platelet count
 - confusion
 - chest pain
 - kidney problems
 - blood clots
 - difficulty breathing
- **If you have aHUS, your doctor will need to monitor you closely during and for at least 12 weeks after stopping treatment for signs of worsening aHUS symptoms or problems related to abnormal clotting (thrombotic microangiopathy).**
Symptoms or problems that can happen with abnormal clotting may include:
 - stroke
 - confusion
 - seizures
 - chest pain (angina)
 - difficulty breathing
 - kidney problems
 - swelling in arms or legs
 - a drop in your platelet count

What are the possible side effects of Soliris?

Soliris can cause serious side effects, including:

- **See “What is the most important information I should know about Soliris?”**
- **Serious allergic reactions.** Serious allergic reactions can happen during your Soliris infusion. Tell your doctor or nurse right away if you get any of these symptoms during your Soliris infusion:
 - chest pain
 - trouble breathing or shortness of breath
 - swelling of your face, tongue, or throat
 - feel faint or pass out

If you have an allergic reaction to Soliris, your doctor may need to infuse Soliris more slowly, or stop Soliris. See “How will I receive Soliris?”

For Discussion with Patients—Important Safety Information (continued)

Common side effects in people with PNH treated with Soliris® include:

- headaches
- runny nose and colds
- sore throat
- back pain
- nausea

Common side effects in people with aHUS treated with Soliris include:

- headache
- diarrhea
- high blood pressure
- common cold (upper respiratory infection)
- abdominal pain
- vomiting
- nasopharyngitis
- low red blood cell count
- cough
- peripheral edema
- nausea
- urinary tract infection
- pyrexia

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of Soliris. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1.800.FDA.1088.

Please see back cover for Important Safety Information.

Please see full prescribing information for Soliris, including boxed WARNING regarding serious meningococcal infection.

General information about Soliris®

Medicines are sometimes prescribed for conditions other than those listed in a Medication Guide. This Medication Guide summarizes the most important information about Soliris. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Soliris that is written for healthcare professionals.

What are the ingredients in Soliris?

Active ingredient: eculizumab

Inactive ingredients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 (vegetable origin) and Water for Injection.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by Alexion Pharmaceuticals, Inc.
352 Knotter Drive, Cheshire, CT 06410 USA.

Revised: 09/2014

Want to learn more about Soliris®?

- Visit www.Soliris.net or www.SolirisREMS.com
- Call 1.888.SOLIRIS (1.888.765.4747) for information regarding Soliris and the Soliris REMS

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See Serious Meningococcal Infections for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747).

The most frequently reported adverse reactions in the PNH randomized trial ($\geq 10\%$ overall and greater than placebo) are: headache, nasopharyngitis, back pain, and nausea.

The most frequently reported adverse reactions in aHUS single arm prospective trials ($\geq 20\%$ combined per patient incidence) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia.

Please see full Prescribing Information for Soliris, including boxed WARNING regarding serious meningococcal infection.

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HEALTHCARE PROVIDER ENROLLMENT FORM

Dear Soliris® (eculizumab) Prescriber,

Alexion, the maker of Soliris, would like to notify you of a Risk Evaluation and Mitigation Strategy (REMS) called the OneSource Safety Support Program (OSSP) to provide important safety information about Soliris.

To get started in the Program, please complete the Prescriber Enrollment Form on the reverse side. The completed Prescriber Enrollment Form can be faxed to the Soliris OneSource Safety Support Program (OSSP) at 1.877.580.2596 (ALXN); scanned and e-mailed to OSSP@alxn.com; or mailed to Alexion Pharmaceuticals, Inc., Attn: OneSource Safety Support Program, 352 Knotter Drive, Cheshire, CT 06410. Enrollment can also be completed online at SolirisREMS.com.

I have received the Soliris educational materials provided through the Soliris OneSource Safety Support Program and I have reviewed information about:

- The need for the patient to receive meningococcal vaccination at least 2 weeks prior to beginning Soliris (eculizumab), unless the risk of delaying Soliris therapy outweighs the risk of developing meningococcal infection
- The risks of developing meningococcal infection while receiving Soliris (eculizumab)

I agree to:

- Review the product labeling and educational materials, and comply with the safety instructions for use, including ensuring meningococcal vaccination status
- Counsel patients (or caregivers, or legal guardians) and provide educational materials to the patient (or caregivers, or legal guardians), including the Soliris Patient Safety Information Card, and the Soliris Medication Guide
- Intend to promptly report cases of meningococcal infection, including the patient's clinical outcomes, by contacting the OneSource Safety Support Program (Alexion Pharmaceuticals, Inc.) at 1.888.SOLIRIS (1.888.765.4747); or reporting the information to the FDA MedWatch Reporting System by phone at 1.800.FDA.1088 (1.800.332.1088) or by mail using Form 3500 at www.fda.gov/medwatch
- Revaccinate patients in accordance with the Advisory Committee on Immunization Practices (ACIP) recommendations for the duration of Soliris therapy

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.
- Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risks of developing a meningococcal infection. (See Serious Meningococcal Infections (5.1) for additional guidance on the management of the risk of meningococcal infection.)
- Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747).

Please complete enrollment form on the reverse side of this letter.

INDICATIONS AND USAGE

Soliris is a complement inhibitor indicated for:

- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- The treatment patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Limitation of Use

Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

CONTRAINDICATIONS

Soliris is contraindicated in:

- Patients with unresolved *Neisseria meningitidis* infection.
- Patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection.

WARNINGS AND PRECAUTIONS

- Discontinue Soliris in patients who are being treated for serious meningococcal infections.
- Use caution when administering Soliris to patients with any other systemic infection.

ADVERSE REACTIONS

- The most frequently reported adverse reactions in the PNH randomized trials ($\geq 10\%$ overall and greater than placebo) are: headache, nasopharyngitis, back pain, and nausea.
- The most frequently reported adverse reactions in aHUS single arm prospective trials ($\geq 20\%$ combined per patient incidence) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia.

Please see full prescribing information for Soliris (eculizumab), including boxed WARNING regarding serious meningococcal infection.

I acknowledge that I have read the above information and agree to comply with the conditions listed when treating a patient with Soliris.

Name (printed): _____

Signature: _____ Date: _____ Title: _____

Office Address: _____ E-mail: _____

City: _____ State: _____ ZIP: _____


Country: _____ Phone Number: _____ Fax Number: _____

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SOLIRISREMS.COM

APPEARS THIS WAY ON ORIGINAL

Prescribing Information | Medication Guide | Important Safety Information



SOLIRIS[®]
(eculizumab)
Concentrated solution for intravenous infusion

SOLIRIS REMS (Risk Evaluation and Mitigation Strategy)

What is the Soliris REMS?

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product.

The purpose of the SOLIRIS REMS is to mitigate the occurrence and morbidity associated with meningococcal infections by informing healthcare providers and patients about the:

- Increased risk of meningococcal infections with Soliris
- Early signs of invasive meningococcal infections, and
- Need for immediate medical evaluation of signs and symptoms consistent with possible meningococcal infections.

Program Requirements

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

HCPs who prescribe Soliris must be specifically certified. Certification consists of review of REMS educational materials and enrollment in the SOLIRIS REMS program.

Healthcare Provider Certification

Certification in the SOLIRIS REMS OneSource Safety Support Program includes the following steps:

1

Review the SOLIRIS REMS HCP Educational Materials:

- [Prescriber Brochure; Important Safety Information about Soliris](#)
- [Dosing and Administration Guide](#)
- [Patient Safety Brochure; Important Safety Information about Soliris](#)
- [Patient Introductory Letter and Voluntary Enrollment Form](#)
- [Soliris Patient Safety Card](#)

2


Enroll in the SOLIRIS REMS Program:


[Click here to complete the SOLIRIS REMS Prescriber Enrollment online](#)


OR

Print and sign the [Prescriber Introductory Letter and Enrollment Form](#)

- Mail the form to OneSource Safety Support Program, Alexion Pharmaceuticals, 352 Knott Drive, Cheshire, CT 06410-9868; or,
- Fax the form to Soliris OneSource Safety Program at 1-877-580-2596 (ALXN); or
- Scan and email the form to OSSP@alxn.com

[Spanish Patient Introductory Letter and Voluntary Enrollment Form](#)

[Spanish Soliris Patient Safety Card](#)

[Spanish Patient Safety Brochure, Important Safety Information about Soliris](#)

The Soliris Patient Safety Card


HCPs should provide their patients with a Soliris Patient Safety Card to carry with them at all times. This safety card contains important safety information about the risk of meningococcal infection that patients need to be aware of before they are given Soliris and during their treatment with Soliris. Remind them to show this card to any doctor involved in their treatment.

HCPs should explain to their patients that if they cannot reach their doctor, they should go to the emergency room **immediately** and show the emergency room staff the Soliris Patient Safety Card. *Even if a patient stops using Soliris*, they should keep their Soliris Patient Safety Card with them for 3 months after the last Soliris dose, since side effects may occur a long time after their last dose of Soliris.


To order a Soliris Patient Safety Information Card, contact OneSource at 1.888.SOLIRIS (1.888.765.4747).

Reporting Adverse Events


HCPs should report all suspected adverse events, including reports of meningococcal infection by contacting the OneSource Safety Support Program (Alexion Pharmaceuticals, Inc.) at 1.888.Soliris (1.888.765.4747); or reporting the information to the FDA MedWatch Reporting System by phone at 1.800.FDA.1088 (1.800.332.1088) or by mail using Form 3500 at <http://www.fda.gov/MedWatch>



Download the PRESCRIBING INFORMATION



Download the MEDICATION GUIDE



SOLIRIS REMS OneSource Safety Support Program

Contact us

Phone:
1.888.SOLIRIS (1.888.765.4747)
Fax: 1.877.580.2596 (ALXN)

Hours of Operation:
Monday - Friday
8:00am-5:00pm
Eastern Time

US Full Prescribing Information | Medication Guide | Important Safety Information | Privacy Notice | Legal Statement

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT C KANE
10/10/2014